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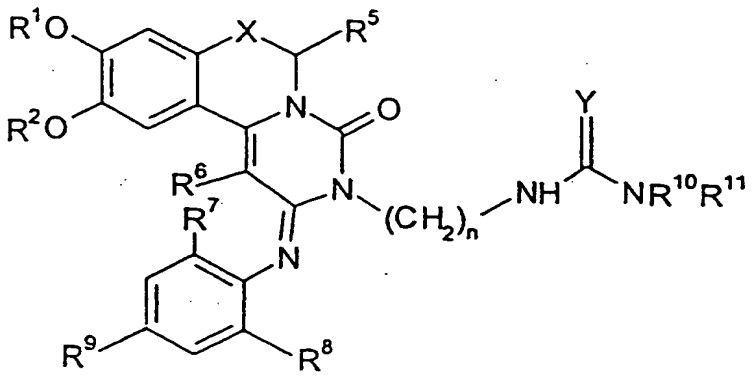
CLAIMS

1. A compound of general formula I:



I

wherein

each of R^1 and R^2 independently represents a C_{1-6} alkyl or C_{2-7} acyl group;

R^5 represents a hydrogen atom or a C_{1-3} alkyl, C_{2-3} alkenyl or C_{2-3} alkynyl group;

R^6 represents a hydrogen atom or a C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, amino, C_{1-6} alkylamino, di(C_{1-6}) alkylamino or C_{2-7} acylamino group;

each of R^7 and R^8 independently represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy, C_{3-6} cycloalkyl; and

R^9 represents a hydrogen or halogen atom or a hydroxy, trifluoromethyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{2-7} acyl, C_{1-6} alkylthio, C_{1-6} alkoxy or C_{3-6} cycloalkyl group;

X represents OCH_2 or a group CR^3R^4, wherein each of R^3 and R^4 independently represents a hydrogen atom or a C_{1-3} alkyl group;

each of R^{10} and R^{11} independently represents a hydrogen atom, a C_{1-3} alkyl, C_{3-6} cycloalkyl or phenyl group;

Y represents an oxygen atom or a group $CHNO_2$, NCN, NH or NNO_2;

n is an integer from 2 to 4;

or a salt thereof.

2. A compound of general formula I wherein, independently or in any compatible combination:

each of R^1 and R^2 represents a C_{1-6} alkyl, preferably a C_{1-4} alkyl, group;

R^1 and R^2 are the same as each other;

each of R^3 and R^4 represents a hydrogen atom;

R^5 represents a hydrogen atom;

R^6 represents a hydrogen atom;

each of R^7 and R^8 represents a C_{1-6} alkyl, preferably methyl, ethyl or isopropyl, group;

R^7 and R^8 are the same as each other;

R^9 represents a halogen atom or a methyl or acetyl group;

Y represents an oxygen atom or a group $CHNO_2$; and

n is 2.

3. 9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-(*N*-carbamoyl-2-aminoethyl)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one.

4. 9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-(*N'*-isopropylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one.

5. 9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*-methyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]-isoquinolin-4-one.

6. 9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N'*-isopropyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]-isoquinolin-4-one.

7. 9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-[1-(*N',N'*-dimethyl-2-nitroethenamine)]-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]-isoquinolin-4-one.

8. 9,10-Dimethoxy-2-(2,4,6-trimethylphenylimino)-3-[*N*-(*N'*-phenylcarbamoyl)-2-aminoethyl]-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-2-one.

9. 9,10-Dimethoxy-3-[2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one.

10. 9,10-Dimethoxy-3-[*N*-(*N'*-nitro)-2-guanidinoethyl]-2-(2,4,6-trimethylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one.

11. 3-[*N*-(*N'*-Cyclohexylcarbamoyl)-2-aminoethyl]-9,10-dimethoxy-2-(2,4,6-trimethyl-phenylimino3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one.

12. 3-(*N*-Carbamoyl-2-aminoethyl)-9,10-dimethoxy-2-(2-methylphenylimino)-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one.

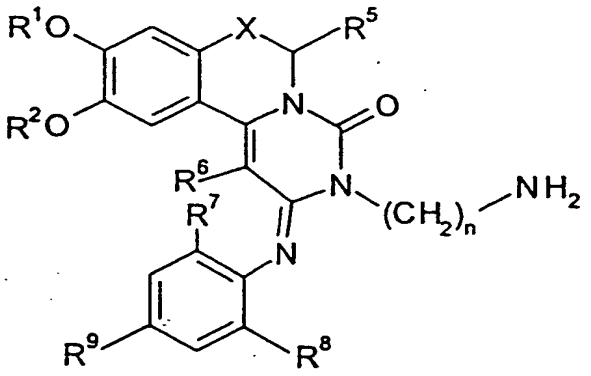
13 3-(*N*-Carbamoyl-2-aminoethyl)-2-(2,6-diisopropylphenylimino)-9,10-dimethoxy-3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one.

14. 3-(*N*-Carbamoyl-4-aminobutyl)-9,10-dimethoxy-2-(2,4,6-trimethylphenylimino)- 3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one.

15. 3-[*N*-(*N*'-Cyano-*N*''-methyl)-2-guanidinoethyl]-9,10-dimethoxy-2-(2,4,6-trimethyl-phenylimino)- 3,4,6,7-tetrahydro-2*H*-pyrimido[6,1-a]isoquinolin-4-one.

16. A process for preparing a compound of general formula I as defined in claim 1, the process comprising:

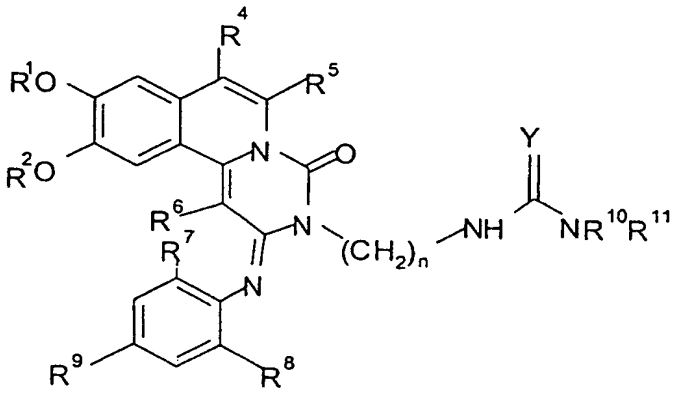
(a) derivatising a compound of general formula II:



II

wherein R^1, R^2, R^5, R^6, R^7, R^8, R^9, X and n are as defined for general formula I, with one or more compounds capable of reacting at the primary amine group of the aminoalkyl moiety (-$(CH_2)_n$-NH_2), to form a compound of general formula I; or

(b) when X in general formula I represents a group CR^3R^4, wherein R^3 represents a hydrogen atom, R^4 represents a hydrogen atom or a C_{1-3} alkyl group, and R^5 represents a hydrogen atom or a C_{1-3} alkyl group, hydrogenating a compound of general formula III:



III

wherein R^1, R^2, R^6, R^7, R^8, R^9, R^{10}, R^{11}, Y and n are as defined for general formula I; and

(c) optionally converting a compound of general formula I so formed into another compound of general formula I.

17. A process as claimed in claim 16, wherein in general formula I, when Y represents an oxygen atom and each of R^{10} and R^{11} represents a hydrogen atom, a compound of general formula II is derivatised with sodium cyanate.

18. A process as claimed in claim 16, wherein in general formula I, when Y represents an oxygen atom, R^{10} represents a hydrogen atom and R^{11} represents a C_{1-3} alkyl, C_{3-6} cycloalkyl or phenyl group, a compound of general formula II is derivatised with an isocyanate of the general formula $R^{11}NCO$.

19. A process as claimed in claim 18, wherein the isocyanate is isopropylisocyanate or phenylisocyanate.

20. A process as claimed in claim 16, wherein in general formula I, when Y represents $CHNO_2$, R^{10} represents a hydrogen atom and R^{11} represents a C_{1-3} alkyl or C_{3-6} cycloalkyl group, a compound of general formula II is derivatised with an N-C_{1-3} alkyl- or N-C_{3-6} cycloalkyl-1-(methylthio)-2-nitroethenamine of the general formula $CH_3SC(=CHNO_2)NR^{10}R^{11}$.

21. A process as claimed in claim 20, wherein the compound of general formula II is derivatised with N-methyl-1-(methylthio)-2-nitroethenamine.

22. A process as claimed in claim 16, wherein in general formula I, when Y represents $CHNO_2$, a compound of general formula II is reacted first with 1,1-bis(methylthio)-2-nitroethylene and the resulting compound is then reacted with an amine of the general formula $R^{10}R^{11}NH$, wherein R^{10} and R^{11} are as defined for general formula I.

23. A process as claimed in claim 22, wherein the amine is isopropylamine or dimethylamine.

24. A process as claimed in claim 16, wherein when in general formula I, Y represents NH, a compound of general formula II is derivatised with a compound of

general formula $CH_3SC(=NH)NR^{10}R^{11}$ or a salt thereof, wherein R^{10} and R^{11} are as defined for general formula I.

25. A process as claimed in claim 16, wherein when in general formula I, Y represents NCN, a compound of general formula II is derivatised with a compound of general formula $CH_3SC(=NCN)NR^{10}R^{11}$ or a salt thereof, wherein R^{10} and R^{11} are as defined for general formula I.

26. A process as claimed in any of claims 16 to 25, wherein the compound of general formula I is as defined in any of claim 1 to 15.

27. A composition comprising a compound of general formula I and a veterinarily or pharmaceutically acceptable carrier or diluent.

28. A composition as claimed in claim27, further comprising an active agent such as a β_2-adrenoceptor agonist or a glucocorticoid steroid.

29. A composition as claimed in claim 27 or claim 28, wherein the composition is a pharmaceutical composition for human medicine.

30. A composition as claimed in claim 27, 28 or 29, adapted for administration by aerosol.

31. A composition as claimed in any of claims 27 to 30, wherein the compound is as defined in any of claims 1 to 15.

32. A compound of general formula I for use in medicine.

33. A compound of general formula I for use as an inhibitor of a phosphodiesterase isoenzyme.

34. A compound of general formula I for use in the prevention or treatment of a disease in which raising the intracellular concentration of cAMP is desirable.

35. A compound of general formula I for use in the prevention or treatment of asthma.

36. A compound of general formula I for use in the prevention or treatment of chronic obstructive pulmonary disease (COPD).

37. A compound as claimed in any of claims 32 to 36, wherein the compound is as defined in any of claims 1 to 15.

38. The use of a compound of general formula I in the manufacture of an inhibitor of a type III/IV phosphodiesterase isoenzyme.

39. The use of a compound of general formula I in the manufacture of a bronchodilator.

40. The use of a compound of general formula I in the manufacture of an anti-asthmatic.

41. The use of a compound of general formula I in the manufacture of a medicament for the prevention or treatment of chronic obstructive pulmonary disease (COPD).

42. The use as claimed in any of claims 38 to 41, wherein the compound is as defined in any of claims 1 to 15.

43. A method for the treatment or prevention of a disease in a mammal where a phosphodiesterase isoenzyme inhibitor and/or a bronchodilator would be expected to be of benefit, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I.

44. A method for the treatment or prevention of asthma in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I.

45. A method for the treatment or prevention of chronic obstructive pulmonary disease (COPD) in a mammal, which method comprises administering to said mammal an effective, non-toxic amount of a compound of general formula I.

46. A method as claimed in claim 43, 44 or 45, wherein the compound is as defined in any of claims 1 to 15.

47. A method as claimed in any of claims 43 to 46, wherein the compound is administered by aerosol.

48. A method as claimed in any of claims 43 to 47, wherein the animal is a human.

49. A compound substantially as hereinbefore described in any of the examples.

50. A process substantially as hereinbefore described in any of the examples.